REMARKS

Applicants wish to thank Examiner Parkin for his time and comments during a teleconference with the undersigned representative on November 1, 2006. The outstanding obviousness rejection was discussed.

Reconsideration of the present application is respectfully requested in view of the Amendment submitted herewith and the following remarks. Claims 20, 21, 23, 24, 26-29, 33, and 34 were pending in the Application. Claims 20, 21, 23, 24, and 26-29 have been cancelled. New claims 35-42 have been added and relate to subject matter previously recited in cancelled claims 20, 21, 23, 24, and 26-29. Claims 33 and 34 have been amended to point out with greater particularity and to claim distinctly certain embodiments of Applicants' invention. Accordingly, upon entry of this Amendment, claims 33-42 are under examination. The Amendment submitted herewith is not to be construed as acquiescence to the stated grounds for rejection and is made without prejudice to prosecution of any subject matter modified or removed by this Amendment in a related divisional, continuation, or continuation-in-part application. No new subject matter has been added. Support for the amended and new claims may be found throughout the specification, for example, at page 11, lines 15-27; and at page 21, lines 4-17.

OBJECTION TO THE CLAIMS

In the Office Action dated May 23, 2006, the Examiner objected to claims 20, 21, 23, 24, and 26-29 under 37 C.F.R. § 1.75(c), asserting that the claims were in improper dependent form. Specifically, the dependent claims did not refer to a preceding independent claim.

Applicants submit that in view of the Amendments submitted herewith, without acquiescence or prejudice, the basis for this objection has been obviated. Claims 20, 21, 23, 24, and 26-29 have been cancelled. New claims 35-42 relate to subject matter previously recited in cancelled claims 20, 21, 23, and 26-29. No new subject matter has been added. Accordingly, Applicants submit that the present claims meet the formality requirements and respectfully request that the objection be withdrawn.

Rejection Under 35 U.S.C. § 103

The Examiner has rejected claims 20, 21, 23, 24, 26-29, 33, and 34 under 35 U.S.C. § 103(a) for allegedly being obvious over Lowell (U.S. Patent No. 5,726,292 (1998)). The Examiner acknowledges that Lowell does not teach generation of a mucosal neutralizing antibody response to "a modified gp160." The Examiner asserts that the modified gp160 is a high molecular weight polypeptide and that Lowell teaches that high molecular weight proteins with endogenous hydrophobic sequences combined with proteosome formulations, when administered intranasally, are capable of inducing a neutralizing mucosal antibody response.

Applicants respectfully traverse this rejection and submit that the presently amended claims are nonobvious. Lowell does not teach or suggest each feature of the present claims; nor does Lowell provide any motivation, teaching, or suggestion that a person having ordinary skill in the art would reasonably expect to achieve successfully Applicants' claimed process.

The present claims are directed to a process for inducing a neutralizing antibody response in a subject against HIV, comprising administering an immunogenic composition directly to mucous membranes, wherein the immunogenic composition comprises (a) an antigen comprising a C-terminal truncated gp160 protein, wherein the C-terminal truncated gp160 protein has a molecular mass of about 140 kDa and comprises the endogenous hydrophobic amino acid sequence set forth at positions 523-551 of SEQ ID NO:1; (b) proteosomes, wherein the proteosomes are complexed or coupled with the antigen; and (c) bioadhesive nanoemulsions, wherein the composition elicits neutralizing antibodies to HIV in a subject upon administration of the composition to the subject, and wherein the neutralizing antibodies are present in one or more of vaginal secretions, intestinal secretions, lung secretions, and feces; and to related processes.

As noted above, the Examiner agrees that Lowell does not teach or suggest "a modified gp160." Lowell specifically does not teach or suggest an antigen that comprises a C-terminal truncated gp160 protein that has a molecular mass of about 140 kDa comprises the endogenous hydrophobic amino acid sequence set forth at positions 523-551 of SEQ ID NO:1, which lacks the transmembrane region of the gp41 portion. Lowell also fails to teach or suggest that the antigen complexed with proteosomes and administered to a subject will elicit

neutralizing antibodies that are detected in at least one of vaginal secretions, intestinal secretions, lung secretions, and feces. Lowell instead teaches that intramuscular injection of full-length gp160 in combination with proteosomes induces production of serum Ig G antibodies that bind to gp160 and to gp41.

The exemplary truncated gp160 polypeptide described in the present application lacks approximately 50% of the gp41 moiety of gp160; however, Lowell fails to teach or suggest that portions of the gp160 may be removed and that the remaining portion would be useful as an immunogenic composition when combined with proteosomes. Furthermore, Lowell points out that gp160 is a transmembrane polypeptide and further describes that the presence of a hydrophobic moiety, such as the transmembrane region of gp160, may be sufficient such that gp160 would form a complex with proteosomes (*see, e.g.*, column 13, lines 43-48; column 18, line 21; column 20, lines 12-16). Because the carboxy terminal truncation of gp160 in the transmembrane gp41 portion would remove one or more hydrophobic portions of transmembrane gp41, a person having ordinary skill in the art could expect that to complex the truncated gp160 polypeptide with proteosomes might require that an exogenous hydrophobic moiety be added to the truncated gp160 to anchor the polypeptide to the proteosomes. As described in the present application, however, the truncated gp160 polypeptide without an exogenous hydrophobic portion in combination with proteosomes was an immunostimulating composition (*see, e.g.*, pages 50-51).

In the HIV art, the antigenicity of the *env* gene products, the precursor gp160 and the mature gp120 and gp41 polypeptides, has been long recognized, and so has the difficulty in identifying one or more epitopes of these envelope proteins that would be useful for immunizing humans against multiple subtypes of HIV (*see, e.g.*, VanCott et al., *J. Immunol. Meth.* 183:103-17 (1995), Introduction and references cited therein (cited reference 23, Information Disclosure Statement submitted July 7, 1999)). Moreover, in the absence of the present application describing use of the truncated gp160 polypeptide, as recited, for inducing a neutralizing antibody response against HIV in a subject, a person having ordinary skill in the art would not reasonably expect to obtain Applicants' claimed invention. The nonobviousness of the presently claimed process is evidenced by VanCott et al. (*J. Immunol.* 160:2000-12 (1998), submitted herewith), who demonstrated that the combination of proteosomes with truncated gp160 was a

significantly improved immunogenic composition compared with full-length gp160 complexed with proteosomes (*see* page 2008, first column; page 2009, Table IV). Even though full-length gp160 elicited neutralizing IgG and IgA that were detected in sera, only mice immunized with truncated gp160 (therein referred to as gp451) elicited neutralizing antibodies in mucosal secretions. VanCott et al. concluded that their findings demonstrated "the importance of both adjuvant and protein structure in eliciting mucosal neutralizing Ab [antibody] responses." (*see* page 2008, last sentence preceding the Discussion). Thus, at the time of filing of the present application, a person having ordinary skill in the art would not have readily predicted which adjuvant in combination with a particular HIV envelope antigen would induce an immune response that is enhanced when compared with the immune response induced by the antigen in the absence of the adjuvant.

Applicants therefore respectfully submit that a *prima facie* case of obviousness has not been established and that the claimed subject matter is nonobvious as required under 35 U.S.C. § 103. Applicants therefore respectfully request that the rejection of the claims be withdrawn.

Applicants respectfully submit that claims 33-42 are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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